



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,572	11/09/2001	Costas D. Maranas	P05413US4	6518
27407	7590	03/22/2004	EXAMINER	
MCKEE, VOORHEES & SEASE, P.L.C. ATTN: PENNSYLVANIA STATE UNIVERSITY 801 GRAND AVENUE, SUITE 3200 DES MOINES, IA 50309-2721			MAHATAN, CHANNING	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/037,572

Applicant(s)

MARANAS ET AL.

Examiner

Channing S Mahatan

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-13 and 15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-13 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>2 Sheets</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

APPLICANTS' ARGUMENTS

Applicants' arguments, filed 06 January 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1, 3-13, and 15. Claims 2 and 14 have been cancelled.

INFORMATION DISCLOSURE STATEMENT

Several references in the 'Information Disclosure Statement', filed 24 November 2003, are lined through. Said references appear to be in duplicate to those that have been previously cited and considered. (Refer to 'Information Disclosure Statement', filed 09 November 2001).

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

Claims 1 and 3-13 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

Art Unit: 1631

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 11, and all claim dependent therefrom are rejected under 35 U.S.C. § 112, first paragraph. The introduction of the following amendment “representation of the plurality of sequences” and “An in vitro method of providing an isolated nucleic acid molecule derived from a directed evolution experiment comprising: providing a nucleotide sequence capable of encoding an amino acid sequence; wherein the nucleotide sequence isolated at least in part through a directed evolution experiment;...” in claim 11 is considered new matter. There did not appear to be any disclosure or contemplation of for the above amendments to claims 1 and 11. None of these concepts were found and none is apparent. Therefore, the amendments to claims 1 and 11 are considered NEW MATTER.

SCOPE OF ENABLEMENT

For reasons of record the rejection of claims 1, 3-13, and 15 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the disclosed method for “predicting the number, type, and distribution of crossovers in directed evolution experiments” such that the “framework provides for determining how fragmentation length, annealing temperature, sequence identity, and number of shuffled parent sequences affect the number, type, and distribution of crossovers along the length of reassembled sequences (page 3, lines 23-27; and pages 5-15), does not reasonably provide enablement for “directed evolution methods/experiments/protocols” by other means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. It should be noted the specification

Art Unit: 1631

discloses the specific language “assembly algorithm”(Abstract; page 25, lines 10 and 22) and it appears the disclosed “reassembly algorithm” (pages 12-14) is the same as the “assembly algorithm”, wherein the assembly algorithm is applied to reassemble a plurality of sequences (i.e. claim 1).

Applicants argue that the specification discloses: 1) at least one method of modeling a directed evolution protocol; and 2) at least one method of excluding silent crossovers (claim 10), therefore, the specification is not required to show it by any other means. This is not agreed with.

The instant claims broadly embrace other means for performing “directed evolution” and therefore, the claims are not commensurate in scope with the disclosure. The specification discloses the general outline of performing “directed evolution” as: 1) Employ equilibrium thermodynamics to quantify annealing event conversions and selectivities (Equation on page 11), wherein the thermodynamics of duplex formation is analyzed by nearest-neighbor parameter which describes the enthalpic and entropic contributions of specific nucleotide pairs in the overlapping region (page 6, lines 7-25; Table on pages 7-8); 2) Calculate a set of recursive relations of the probability that a full-length reassembled sequence of B nucleotides has x crossovers (Equation on page 12), wherein the probability that a given position I in a reassembled sequence is the site of crossover (pages 12-15; and Figure 2). No other procedures are disclosed for performing “directed evolution”. None of the outlined steps or elements are limitations of the instant claims. The specification does not provide guidance, direction, or examples as to other ways of performing “directed evolution”. The specification does not

Art Unit: 1631

provide guidance, direction, or examples as to other types procedures for “directed evolution” (i.e. methods, experiments, protocols).

The instant claims broadly embrace other means for “excluding silent crossovers” and therefore, the claims are not commensurate in scope with the disclosure. Again, the disclosure indicates “if the annealing of a fragment m to a growing template ending with a fragment from parent k is equivalent to the continuation of the template with the nucleotides from parent k, no crossover is counted” (page 13, lines 13-22; and page 17, lines 13-16). No other procedures are disclosed for “excluding silent crossovers”. This element is not a limitation of the instant claims. The specification does not provide guidance, direction, or examples as to other ways of “excluding silent crossovers”. The specification does not provide guidance, direction, or examples as to other types procedures for “excluding silent crossovers”.

Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

Claims 1 and 3-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

VAGUE AND INDEFINITE

Claim 1 and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is a “A computer-based directed evolution method...”, however, the claim

Art Unit: 1631

recites a final step “providing a representation of the plurality of sequences”. There is no indication of when the “directed evolution method” is achieved as implied by the preamble. While minor details are not required in method/process claims, at least the basic step must be recited in a positive/active fashion. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 1 and all claims dependent therefrom recite the step “providing a representation of the plurality of sequences” which is vague and indefinite. It is unclear if the representation is of the plurality of sequences in the “applying thermodynamic...to determine statistics of hybridization” or is the representation of the plurality of sequences in the “applying the assembly algorithm to reassemble” step. Clarification of the metes and bounds, via clearer claim language, is requested.

LACK OF ANTECEDENT BASIS

Claims 6 and 7 recite the limitation “the directed evolution protocol” which lacks proper antecedent basis. Claim 1, from which claims 6 and 7, depend from does not indicate a “directed evolution protocol”.

ACTION IS FINAL, AS NECESSITATED BY AMENDMENT

Applicants’ amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after

Art Unit: 1631

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina M. Plunkett, whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Application/Control Number: 10/037,572

Page 8

Art Unit: 1631

Date:

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER

3/8/04

Examiner Initials:

AP/1631